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Patient reported outcome measures for allergy and asthma in children

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Abstract

There is increasing recognition of the importance of patient's perceptions of disease and their assessments of health care processes. Patient-reported outcome measures (PROMs) are therefore now regarded as at least as important as the traditional objective measures of disease. For minors, parental and, except in the very young and severely cognitively impaired, the child's perspectives are important because they provide unique and complementary information. In this review, we summarise the evidence on PROMs for allergy and asthma for use in children.

Overall, there are fewer PROMs available for use in children than in adults. We were able to identify some validated pediatric PROMs that have been developed for use in atopic eczema/dermatitis, food allergy, allergic rhinitis/rhinoconjunctivitis and asthma. There is very limited evidence on deploying these instruments out with research settings. There is therefore a pressing need to report on the experiences of using PROMs for allergy and asthma in routine clinical care. In particular, there is a need to understand how acceptable these are to children/carers, whether they can be incorporated into routine clinical assessments and if they are responsive to changes in treatment made in routine clinical practice.

Introduction

Over recent decades, there has been a major shift in clinicians and researchers' understanding of the impact of disease and clinical interventions on patients (1, 2). Traditionally, this understanding was rooted in a 'disease-centred' paradigm, whereby the impact of diseases was primarily authenticated through objective measures and clinical criteria (1, 2). However, more recently, we have seen an important paradigm shift towards more patient-centred care (3). This new perspective emphasises the importance of subjective dimensions and patient perceived notions of disease and the impact of clinical interventions on their day-to-day well-being (1-3). There is now a greater recognition that disease and the clinical encounter are perceived not only in terms of objective targets, but that these need to be understood together with patients' perceptions of their condition, which are influenced and/or reinforced by their beliefs, experiences and cultural realities (1-3). Consequently, the outcomes of clinical interventions obtained based on patient reports without involvement or interpretation of a physician, commonly known as patient-reported outcome measures (PROMs), should be considered as at least as important as more traditional objective assessments (1, 4).

In this paper, drawing on our recent rigorously conducted systematic reviews, systematic reviews from other investigators, and key recent evidence-based guidelines from the European Academy of Allergy and Clinical Immunology (EAACI) and the Global Allergy and Asthma European Network (GA2LEN), we provide an overview of the current evidence on PROMs for allergy and asthma in children (1, 5-8). We focus on the clinically relevant and validated PROMs that are now used for

atopic eczema, food allergy, allergic rhinitis and asthma. We have deliberately steered clear of discussing PROMs that have not been validated as these may not accurately reflect patient perceptions of their conditions. We highlight the key features of these validated instruments and discuss future developments that may enhance their usefulness.

Definition of PROMs

There is no universally accepted definition of PROMs, but we will here adopt a definition we had earlier proposed (see Box 1) (6). PROMs are used to assess a range of outcomes primarily from clinical trials assessing the impact of illness or clinical interventions; these include health or functional status, health-related quality of life, perception of symptoms, well-being, satisfaction with treatment, and perceptions of the quality of care (6, 9).

The importance of PROMs in the context of allergy and asthma

The importance of collecting data on PROMs during clinical trials and, more recently, routine clinical encounters has been advocated by leading global health institutions, including the World Health Organization (WHO), the United States Food and Drug Administration (FDA), and the European Medicines Agency (EMA) (3, 10, 11).

Asthma is now the commonest long-term condition among children (12). Together with other allergic disorders, such as atopic eczema/dermatitis, allergic rhinitis, food allergy and asthma, these conditions constitute a considerable burden on the daily lives of many children and their families (13). In addition, whilst several therapeutic regimens have been developed to manage allergic disorders and asthma, adherence to recommended regimens may also have substantial impact on the day-to-day lived experience of children and their parent/caregivers (5). For example, decisions surrounding the use of adrenaline (epinephrine) in the context of managing anaphylaxis or inhalers for asthma control may have a negative impact on the child or their parents/caregivers (5). Capturing children's or parents'/caregivers' perception of the impact of allergic disorders and asthma and the impact of treatments will help support improved decision-making by clinicians and help researchers better design interventions that target improvement of the overall quality of life of children and their families (1, 5, 6). The World Allergy Organization (WAO), EAACI and GA²LEN therefore now also recommend that PROMs should be routinely collected in allergy and asthma clinical trials (1, 7).

Generic and disease-specific instrument

Over 3,000 generic and disease-specific PROMs currently exist, these now commonly being used in research, particularly in clinical trials (6). Generic PROMs are instruments that assess patients' perception across a number of diseases at the same time without having a particular disease as their primary focus. Disease-specific are in contrast instruments that assess patients' perception on

one specific disease. Whilst generic PROMs may allow comparison of patient perceptions across different diseases, unlike disease-specific PROMs they do not allow detailed picture of patient perceptions of specific diseases to emerge; furthermore, they typically fail to capture changes in patients' everyday concerns related to their disease status (1, 5, 6). An additional advantage of disease-specific PROMs over generic PROMs is that they are more sensitive in estimating the burden of disease and capturing the impact of interventions (1, 5, 14).

Existing validated disease-specific PROMs for allergy and asthma in children

Most existing validated disease-specific PROMs for allergy and asthma have been developed for the adult population. Key features of the available validated disease-specific PROMs for allergy and asthma in children are summarized in Table 1.

PROMs for atopic eczema/dermatitis in children

A recent systematic review identified one validated PROM for children with atopic eczema/dermatitis: the Infant's Dermatitis Quality of Life Index (IDQoL) (8). This tool was developed in 2001 and it is intended to be completed by parents or caregivers to assess the impact of atopic dermatitis on the Quality of Life (QOL) of children below the age of four years (15, 16). The IDQoL has been extensively validated and used in several studies, now translated into 21 languages and used in 18 countries; it contains 10 questions, each question scoring a minimum of zero and maximum of three.

PROMs for food allergy in children

From our previous systematic review (5), which contributed to the development of the EAACI guideline on food allergy health related QOL measures (7), we identified three core food allergy-specific PROMs for the pediatric population, all measuring the QOL of children with food allergy. These have been validated in several studies (5). The instruments are: (a) Food Allergy Quality of Life Questionnaire (FAQLQ); (b) Food Allergy Quality of Life Assessment Tool for Adolescents (FAQL-teen); and (c) You and Your Food Allergy. The detail appraisal of these instruments and the results of the studies validating their performance are presented in that review (5). The FAQLQ instrument was originally developed in Dutch. It is divided into two: FAQLQ-Child Form and FAQLQ-Teenager Form. The FAQLQ-Child Form is intended for children aged 8-12 years and contains 24 self-reported items and four domains. The FAQLQ-Teenager Form is intended for children aged 13-17 years and contains 28 self-reported items and three domains. The FAQL-teen instrument was developed in the United States and intended for children aged 13-19 years; it contains 17 self-reported items. You and Your Food Allergy instrument was developed in the UK for children aged 13-18 years, containing 34 self-reported items, which are divided into five domains (5).

PROMs for allergic rhinitis/rhinoconjunctivitis in children

We identified two validated disease-specific PROMs for assessment of disease-specific QOL in children with allergic rhinitis or rhinoconjunctivitis: (a) the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ)(17) and (b) the Adolescent Rhinoconjunctivitis Quality of Life Questionnaire (AdoIRQLQ) (18). Both PRQLQ and AdoIRQLQ were originally developed to be applied in North America. The PRQLQ contains 23 question items in five domains and it is intended to be self-completed by children aged 6-12 years. The AdoIRQLQ contains 25 question items in six domains and it is intended to be self-completed by children aged 12-17 years

PROMs for asthma in children

For asthma, our previous systematic review identified four validated asthma-specific PROMs for children (6). These include: (a) the Pediatric Asthma Quality of Life Questionnaire (PAQLQ); (b) Childhood Asthma Control Test (C-ACT); (c) Childhood Asthma Questionnaire (CAQ); and (d) Pediatric Asthma Quality of Life (PedsQL). Our detailed appraisals of these instruments are presented in that paper (6).

The PAQLQ is derived from the Asthma Quality of Life Questionnaire (AQLQ) originally designed for use in adults (19, 20); it is intended to measure the functional impairments of children with asthma. Although our appraisal showed that only few validation studies have been undertaken to assess the validity of PAQLQ, it is the only PROM that comprehensively addresses asthma-related QOL in children with asthma.

The C-ACT measures the degree of asthma control in children and our appraisal indicated that although it offers promise for this purpose, further validation work is required to be undertaken considering concerns about whether it adequately measures poorly controlled asthma (6). The CAQ was developed to measure the quality of life of children with asthma, but our appraisal showed that it has been poorly validated (6).

The PedsQL is a generic instrument but has disease-specific modules, including a module for asthma, which is also intended to measure the QOL in children with asthma. Our appraisal indicated that the development of the PedsQL was inadequate and there was wide variation in its performance; the asthma module was particularly poorly described, thus its application for assessing the QOL of children with asthma appears largely inadequate (6).

Challenges of incorporating PROMs into routine care and areas for further research and development

Most of the evidence in relation to use of PROMs in the context of allergy and asthma in children comes from clinical research studies. There is therefore very little evidence in relation to their routine deployment in clinical practice (21). Key challenges in using these clinically are likely to

relate to awareness of which validated instruments are available, which to select when a choice exists, the frequency with which these should be used, the burden on children/carers associated with completing these, and how best to incorporate the findings from these instruments into routine care (22-24). There is therefore the need for important health services research to provide answers to these and related questions pertaining to routine clinical use of allergy and asthma PROMs in children.

Moreover, there is a need to ensure that there is a comprehensive suite of PROMs available for use across the range of clinical presentations of allergy in children, and that these are available both for completion by affected children and carers. There is therefore the need for further development work in relation to conditions such as venom allergy, urticaria and angioedema. It is also important that these tools are available across all childhood age groups and in a range of languages suitable for use in multicultural populations.

Conclusions

Whilst there is an increasing recognition of the importance of integrating PROMs in clinical practice and as part of the outcomes assessed when evaluating the impact of diseases and clinical interventions in clinical research, progress has been slow in incorporating PROMs for allergy and asthma into the routine clinical care of children. We have in this paper identified available validated PROMs for use in children and summarized their key properties (Table 1). This we hope should provide both physicians and researchers an accessible summary of the available instruments and whom it is appropriate to use these in. We have also through so doing highlighted gaps where no suitable instruments exist, and these should be seen as priority areas for further development. More generally, we have highlighted the need for a focused effort on developing the evidence base in relation to the opportunities and challenges with deploying PROMs for allergy and asthma in the routine clinical care of children.

References

- 1 Baiardini I, Bousquet PJ, Brzoza Z, *et al.* Recommendations for assessing patient-reported outcomes and health-related quality of life in clinical trials on allergy: a GA(2)LEN taskforce position paper. *Allergy*. 2010; **65**: 290-5.
- 2 Nelson EC, Eftimovska E, Lind C, Hager A, Wasson JH, Lindblad S. Patient reported outcome measures in practice. *BMJ (Clinical research ed)*. 2015; **350**: g7818.
- 3 WHO. Primary health care – now more than ever. *The World Health Report 2008*. Geneva: World Health Organization 2008.
- 4 Anker SD, Agewall S, Borggrefe M, *et al.* The importance of patient-reported outcomes: a call for their comprehensive integration in cardiovascular clinical trials. *European heart journal*. 2014; **35**: 2001-9.
- 5 Salvilla SA, Dubois AE, Flokstra-de Blok BM, *et al.* Disease-specific health-related quality of life instruments for IgE-mediated food allergy. *Allergy*. 2014; **69**: 834-44.

- 6 Worth A, Hammersley V, Knibb R, *et al.* Patient-reported outcome measures for asthma: a systematic review. *NPJ primary care respiratory medicine*. 2014; **24**: 14020.
- 7 Muraro A, Dubois A, DunnGalvin A, *et al.* EAACI Food Allergy and Anaphylaxis Guidelines. Food allergy health- related quality of life measures. *Allergy*. 2014; **69**: 845-53.
- 8 Heintz D, Chalmers J, Nankervis H, Apfelbacher C. Eczema Trials: Quality of Life Instruments Used and Their Relation to Patient-reported Outcomes. A Systematic Review. *Acta dermato-venereologica*. 2015.
- 9 Black N, Jenkinson C. Measuring patients' experiences and outcomes. *BMJ (Clinical research ed)*. 2009; **339**: b2495.
- 10 U. S. Department of Health Human Services, Research FDACfDE, U. S. Department of Health Human Services, Research FCfBE, U. S. Department of Health Human Services, Health FCfDR. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health and quality of life outcomes*. 2006; **4**: 79-79.
- 11 Committee for Medicinal Products for Human Use (CHMP). Reflection paper on the regulatory guidance for the use of health-related quality of life (HRQoL) measures in the evaluation of medicinal products. London, UK: European Medicines Agency 2005.
- 12 Beasley R, The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *The Lancet*. 1998; **351**: 1225-32.
- 13 O'connell E. The burden of atopy and asthma in children. *Allergy*. 2004; **59**: 7-11.
- 14 Rothman ML, Beltran P, Cappelleri JC, Lipscomb J, Teschendorf B, the Mayo FDAP-ROCMG. Patient-Reported Outcomes: Conceptual Issues. *Value in Health*. 2007; **10**: S66-S75.
- 15 Lewis- Jones M, Finlay A, Dykes P. The infants' dermatitis quality of life index. *British Journal of Dermatology*. 2001; **144**: 104-10.
- 16 Basra M, Gada V, Ungaro S, Finlay AY, Salek S. Infants' Dermatitis Quality of Life Index: a decade of experience of validation and clinical application. *British Journal of Dermatology*. 2013; **169**: 760-68.
- 17 Juniper EF, Howland WC, Roberts NB, Thompson AK, King DR. Measuring quality of life in children with rhinoconjunctivitis. *Journal of allergy and clinical immunology*. 1998; **101**: 163-70.
- 18 Juniper EF, Guyatt GH, Dolovich J. Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *Journal of allergy and clinical immunology*. 1994; **93**: 413-23.
- 19 Juniper EF, Guyatt G, Epstein R, Ferrie PJ, Jaeschke R, Hiller TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax*. 1992; **47**: 76-83.
- 20 Juniper E, Guyatt G, Cox F, Ferrie P, King D. Development and validation of the mini asthma quality of life questionnaire. *European Respiratory Journal*. 1999; **14**: 32-38.
- 21 Dawson J, Doll H, Fitzpatrick R, Jenkinson C, Carr AJ. The routine use of patient reported outcome measures in healthcare settings. *British Medical Journal*. 2010; **340**.
- 22 Meadows KA. Patient-reported outcome measures: an overview. *Br J Community Nurs*. 2011; **16**: 146-51.
- 23 Smith PC, Street AD. On the uses of routine patient-reported health outcome data. *Health Economics*. 2013; **22**: 119-31.
- 24 Rombach I, Rivero-Arias O, Gray AM, Jenkinson C, Burke Ó. The current practice of handling and reporting missing outcome data in eight widely used PROMs in RCT publications: a review of the current literature. *Quality of Life Research*. 2016: 1-11.

Box 1: Definition of a PROM (6)

“A PROM for a long-term condition is a measure of the impact and/or the outcome of treatment for that condition on a patient's quality of life, reported directly by the patient or carer. This may include impact of the condition on health-related quality of life, perceptions of health/functional status related to the long-term condition and the impact of treatment/care on the patient's quality of life”

Table 1 Characteristics of existing validated patient reported outcome measures (PROMs) for allergy and asthma in children

Instrument	Target population	Number of items and domains	Mode of administration	Time to complete	Original language
<i>PROM for atopic eczema/dermatitis</i>					
Infant's Dermatitis Quality of Life Index (IDQoL)	Children with atopic eczema/dermatitis below the aged of 4 years	10 items, domains not indicated	Parent/caregiver-completed	2-3 min	English
<i>PROMs for food allergy</i>					
Food Allergy Quality of Life Questionnaire (FAQLQ): FAQLQ-Child Form (FAQLQ-CF) FAQLQ-Teenager Form (FAQLQ-TF)	FAQLQ-CF for children aged 8-12 years FAQLQ-TF for adolescents aged 13-17 years	FAQLQ-CF: 24 items in four domains: allergen avoidance; risk of accidental exposure; emotional impact; and dietary restrictions FAQLQ-TF: 28 items in three domains: allergen avoidance and dietary restrictions; emotional impact; and risk of accidental exposure	FAQLQ-CF: self-completed by child FAQLQ-TF: self-complete by adolescent	Not indicated	Dutch
Food Allergy Quality of Life Assessment Tool for Adolescents (FAQL-teen)	Adolescents aged 13-19 years	17 items, domains not indicated	Self-completed by adolescent	Not indicated	Dutch

Instrument	Target population	Number of items and domains	Mode of administration	Time to complete	Original language
You and Your Food Allergy	Teenagers aged 13-18 years	34 items in five domains: social well-being and independence; support; day-to-day activities; family relations; and emotional well-being	Self-completed by teenager	Not indicated	English
<i>PROMs for allergic rhinitis/rhinoconjunctivitis</i>					
Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ)	Children with allergic rhinitis/rhinoconjunctivitis aged 6-12 years	23 items in 5 domains: nose symptoms, eye symptoms, practical problems, activity limitation and other symptoms	Self-completed	Not indicated	English
Adolescent Rhinoconjunctivitis Quality of Life Questionnaire (AdoIRQLQ).	Children with allergic rhinitis/rhinoconjunctivitis aged 12-17 years	25 items in six domains: nose symptoms, eye symptoms, practical problems, activity limitation, non-hayfever symptoms and emotional function	Self-completed	Not indicated	English
<i>PROMs for asthma</i>					

Instrument	Target population	Number of items and domains	Mode of administration	Time to complete	Original language
Pediatric Asthma Quality of Life Questionnaire (PAQLQ)	Children with asthma aged 7-17 years	23 items in 3 domains: 10 items for symptoms 5 items for activity 8 items for emotional function	Self- or interviewer-completed	10-15 min	English
Childhood Asthma Control Test (C-ACT)	Children with asthma aged 4-11 years	7 items in 2 domains: 4 items for child 3 items for caregiver	Self-completed (child), and caregiver	Not indicated	English
Childhood Asthma Questionnaire (CAQ);	CAQ-A children 4-7 years CAQ-B children 8-11 years CAQ-C children 12-16 years	CAQ-A 14 items, domains not indicated CAQ-B 23 items, domains not indicated CAQ-C 46 items, domains not indicated	Self-completed, with parental assistance if required	10-20 min	English
PedsQL	Children and adolescents aged 2-18 years	Generic core: 23 items in 4 domains Asthma module: 28 items in 4 domains: 11 items for symptoms 11 items for treatment problems 3 items for worry 3 items for communication			

Competing interests

None

Authors' contributions

This was an invited review. AS conceived the topic. IS and BN drafted the manuscript, which was then revised after several rounds of critical comments from AS. All authors read and approved the manuscript.

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